The Novel Use of Different Bupivacaine Preparations with Combined Regional Techniques for Postoperative Pain Management in Non-Opioid Based Laparoscopic Inguinal Herniorrhaphy

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Brief Abstract:

Opioids are important for surgical pain control but may not be appropriate for patients with narcotic abuse histories or opioid intolerance. We describe a laparoscopic bilateral inguinal herniorrhaphy performed without perioperative or postoperative narcotics. Postoperative analgesia involves a novel technique using two different bupivacaine formulations that act synergistically to avoid lag time and provide extended pain relief during the acute surgical recovery phase.

Keywords:
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Introduction:

Opioids have historically been a first-line therapy for surgical pain control, both in the setting of the operating theater as well for postoperative pain relief. However, the standard use of opioids has come at a cost of widespread opioid tolerance or abuse, and thus may not be appropriate for patients with narcotic abuse histories. Such challenges require surgeons and anesthesiologists to look for novel non-opioid alternatives to treat surgical pain.

Use of injectable local anesthetics has been well established to decrease operative and postoperative pain. Standard bupivacaine HCl has a fast onset of action, but the anesthetic effects only last 4-8 hours, making it ineffective for prolonged postoperative pain relief. Adding dexamethasone to bupivacaine HCl has the effect of extending the duration of action to over 20 hours.[1] A newer agent that has been used successfully in the surgical setting for extended postoperative analgesia is injectable liposomal bupivacaine (LB). LB has a duration up to 96 hours,[2] which is effective for ambulatory surgeries; however, it has a much longer duration of onset than bupivacaine HCl and may take hours to achieve therapeutic effects. We hypothesized that using both bupivacaine HCl and LB would allow for pain relief in the immediate postoperative phase without the lag in onset that can result from LB alone.

We describe a laparoscopic totally extraperitoneal (TEP) bilateral inguinal herniorrhaphy performed without perioperative or postoperative narcotics in a multimodal approach. Our principal technique for managing postoperative pain relies on a novel regional anesthetic technique through bilateral transversus abdominis plane (TAP) blocks with LB, administered in concert with bupivacaine HCl/dexamethasone instilled in the preperitoneal space.

Materials and Methods:

A 57 year old African-American male presented to our outpatient surgery clinic for evaluation of symptomatic fat-containing bilateral inguinal hernias with chronic groin pain. His past medical history was significant for morbid obesity (152 kg, BMI 50.2), diabetes mellitus, chronic obstructive pulmonary disease, and past abuse of alcohol and crack cocaine, from which he had been abstinent over 18 months. He was in a recovery program which provided housing and employment assistance, but as part

of his program he was prohibited from testing positive for any narcotics. He was scheduled for laparoscopic bilateral inguinal herniorrhaphy via TEP approach.

In consultation with Anesthesiology, a narcotic-free surgical and post-surgical regimen was planned. General anesthesia was induced with midazolam 2 mg IV, ketamine 50 mg IV, and, propofol 200 mg IV. Succinylcholine 200 mg IV was used to facilitate tracheal intubation. After induction of general anesthesia, a dexmedetomidine infusion was started at 0.4 mcg/kg/hr and maintained throughout the perioperative period (100 mcg IV total). The patient was ventilated with 100% oxygen. Sevoflurane was added to maintain anesthesia perioperatively. Neuromuscular blockade for the surgery was provided with cisatracurium (28 mg IV total). Neostigmine/glycopyrrolate (5mg/1 mg IV) was used at the conclusion of the surgery to reverse the neuromuscular blockade. Ondansetron 4 mg IV was administered for antiemetic prophylaxis prior to emergence from anesthesia. Intravenous ketorolac 30 mg and acetaminophen 1000 mg were administered for adjunctive pain control during the case.

Prior to transversus abdominis plane (TAP) block infiltration, 20 mL of liposomal bupivacaine (266mg; 13.3mg/mL) was mixed with 4 mg of dexamethasone in 35 mL 0.9% injectable normal saline and 5 mL 0.25% bupivacaine HCl for a total of 60 mL. Under sterile technique with ultrasound guidance, a bilateral TAP block was performed with injection of 30 mL of the LB/dexamethasone mixture per side.

A standard laparoscopic TEP bilateral inguinal hernia repair was then started. A total of 10 mL of 0.25% bupivacaine HCl with 1:200,000 epinephrine was injected into the port sites prior to incision. A complete preperitoneal dissection was performed with reduction of bilateral indirect inguinal fat-containing hernias and bilateral placement of 14x15 cm polypropylene mesh fixated with absorbable tacks. A total of 30 mL 0.25% bupivacaine HCl with 4 mg dexamethasone was then instilled directly into the "Triangles of Pain" bilaterally, just lateral to the testicular structures. There were no immediate postoperative complications. The patient was then discharged on oral ibuprofen and acetaminophen every 6 hours as needed. Pain scores were obtained in the PACU on postoperative day 0 and by telephone calls on POD 1, 2, and 3.

Results:

There were no complications secondary to anesthesia, block placement, or herniorrhaphy. The patient's subjective pain score in PACU was 0 on a 10-point scale. On POD 1 he had mild pain rated at 4/10, requiring ibuprofen 600 mg and acetaminophen 2000 mg in 24 hours. Pain on POD 2 was slightly higher at 5/10, worse with movement, but he stated "pain is not bad and is very tolerable." He required ibuprofen 1800 mg and acetaminophen 4000 mg. Per the patient, postoperative pain relief from the block wore off the morning of POD 2 and lasted approximately 44 hours. On POD 3 pain had decreased to 3/10 and was only present with movement. He required ibuprofen 1800 mg and acetaminophen 3000 mg with good relief. He was satisfied with his surgical result and was able to return to work.

Discussion:

While laparoscopic inguinal hernia repair has long been considered superior to the open approach with respect to postoperative pain and faster return to work,[3] as a surgical procedure it is still likely to cause significant patient discomfort in the immediate postoperative phase. Common surgical practice is to prescribe narcotic pain medications for postoperative pain. However, patients with opioid abuse histories or tolerance merit more detailed consideration for their surgical pain management. From a public health perspective, avoiding opioids for surgical pain should be pursued whenever possible, and this necessitates not only minimally-invasive procedures when indicated, but also use of

non-narcotic agents during and after surgery. Our patient's case is especially notable as he was prohibited by his recovery program to have any form of narcotics, despite his scheduled surgery.

It has been reported that transversus abdominis plane (TAP) blocks and local anesthetic infiltration (LAI) provide comparable short-term postoperative analgesia in lower abdominal surgeries.[4] Preliminary results from one of our current studies examining postoperative analgesia in laparoscopic TEP inguinal herniorrhaphy suggests that TAP blocks and preperitoneal instillation of local anesthetics provide comparable postoperative analgesia. Since it has been reported that TAP blocks provide a better long-lasting effect in lower abdominal surgeries compared to LAI,[5] we decided to use a liposomal bupivacaine (LB) preparation in the TAP blocks.

Liposomal bupivacaine contains a small amount of extra-liposomal bupivacaine (about 3 %) to allow for fast onset, similar to bupivacaine HCl.[6] However, this would only account for roughly 2.5 mg of bupivacaine HCl in a 133 mg LB injection per abdominal infiltration. Although it is reported that LB exhibits time-to-onset characteristics similar to traditional bupivacaine HCl in a cutaneous pain model,[7] our clinical experience in more invasive surgeries (total knee arthroplasty, total hip arthroplasty, colectomies, open inguinal herniorrhaphy, and ventral hernia repairs) have not found this to be true. LB exhibits a bimodal release profile with an initial peak soon after administration, followed by a later peak (associated with release of the liposome-encapsulated bupivacaine) that occurs within 10 to 36 hours after administration.[8] From our clinical experience, an additional administration of bupivacaine HCl is required to bridge the onset of the second peak (10-36 hours after administration) of LB for clinically effective anesthesia. Though there are concerns over possible local anesthetic toxicity with supplementary bupivacaine HCl dosing, additional bupivacaine HCl – up to 50% of the total LB dose – may be administered without adverse effects.[9]

Rather than mix a large amount of bupivacaine HCl with LB in the patient's TAP blocks, we chose a combination of LB TAP blocks with preperitoneal infiltration of bupivacaine HCl mixed with dexamethasone. During preperitoneal dissection in a laparoscopic TEP inguinal herniorrhaphy, the "Triangle of Pain" – an anatomic region bordered superiorly by the iliopubic tract, medially by the testicular vessels, and laterally by the psoas and abdominal wall – is exposed. The Triangle of Pain contains the ilioinguinal nerve, lateral femoral cutaneous nerve, and genital branch of the genitofemoral nerve. Bathing these nerves with local anesthetic can help decrease postoperative pain, though studies suggest bupivacaine HCl alone is ineffective in long-term pain relief.[10] **[IMAGE 1]** Preliminary studies at our institution examining a bupivacaine/dexamethasone mixture in this region have shown extended pain relief with the addition of dexamethasone, and thus it can provide enough analgesia until the second peak of liposomal bupivacaine takes effect. The use of a traditional "rapid onset-limited duration" local anesthetic in conjunction with a novel "slower onset-extended duration" local anesthetic preparation in a tandem manner along the relevant pain pathways appears to enhance the quality of analgesia in the immediate and extended postoperative period without the increased risk of toxicity or potential complications of indwelling catheters, while possibly improving the patient's overall recovery and convalescence.

Our results show that short- and long-acting local anesthetic agents may be used synergistically to avoid lag time and provide extended pain relief during the acute surgical recovery phase. A combined regional technique with different bupivacaine formulations in coordination with multimodality non-opioid analgesics is a feasible alternative for surgical pain control in laparoscopic bilateral inguinal herniorrhaphy.

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IMAGE 1: Preperitoneal instillation of local anesthesia (PILA) performed via direct injection through surgical instrumentation. The bupivacaine/dexamethasone mixture is administered lateral to the testicular structures, inferior to the iliopubic tract, affecting the ilioinguinal, lateral femoral cutaneous, and genitofemoral nerves.

References:

[1] Fanzca F, Danesh-Clough TK, White R. Adjuvant dexamethasone for bupivacaine sciatic and ankle blocks: results from 2 randomized placebo-controlled trials. *Reg Anesth Pain Med* 2013;38(4):300-307.

[2] Candiotti K. Liposomal bupivacaine: An innovative nonopioid local analgesic for the management of postsurgical pain. *Pharmacotherapy* 2012;32:19S-26S.

[3] McCormack K, Wake B, Perez J, Fraser C, Cook J, McIntosh E, Vale L, Grant A. Laparoscopic surgery for inguinal hernia repair: systematic review of effectiveness and economic evaluation. *Health Technol Assess* 2005;9(14):1-203.

[4] Yu N, Long X, Lujan-Hernandez JR, Succar J, Xin X, Wang, X. Transversus abdominis-plane block versus local anesthetic wound infiltration in lower abdominal surgery: a systematic review and meta-analysis of randomized controlled trials. *BMC Anesthesiology* 2014;14:121-9.

[5] Yu N, Long X, Lujan-Hernandez JR, Succar J, Xin X, Wang, X. Transversus abdominis-plane block versus local anesthetic wound infiltration in lower abdominal surgery: a systematic review and meta-analysis of randomized controlled trials. *BMC Anesthesiology* 2014;14:121-9.

[6] Hu D, Onel E, Singla N, Kramer WG, Hadzic A. Pharmacokinetic profile of liposome bupivacaine injection following a single administration at the surgical site. *Clin Drug Investig* 2013;33:109–115.

[7] Apseloff G, Onel E, Patou G. Time to onset of analgesia following local infiltration of liposome bupivacaine in healthy volunteers: a randomized, single-blind, sequential cohort, crossover study. *Int J Clin Pharmacol Ther* 2013;51:367-73.

[8] Hu D, Onel E, Singla N, Kramer WG, Hadzic A. Pharmacokinetic profile of liposome bupivacaine injection following a single administration at the surgical site. *Clin Drug Investig* 2013;33:109–115.

[9] EXPAREL [prescribing information]. Parsippany, NJ: Pacira Pharmaceuticals, Inc.; 2011.

[10] Tong YS, Wu CC, Bai CH, Lee HC, Liang HH, Kuo LJ, Wei PL, Tam KW. Effect of extraperitoneal bupivacaine analgesia in laparoscopic inguinal hernia repair: a meta-analysis of randomized control trials. *Hernia* 2014;18(2):177-183.